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PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

James **CASTILLO**

Application No.: **09/954,494** Examiner: **Kim, Vickie**

Filed: **September 17, 2001** Group Art Unit: **1614**

For: **ALCOHOL BASED TOPICAL ANESTHETIC FORMULATION AND METHOD**

Attorney Docket: **3863.015**

SUPPLEMENTAL DECLARATION UNDER 37 C.F.R. §1.132

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

I, James Castillo, 15412 15th Street, Lutz Florida 33549, declare and state the following:

In March of 1980, I graduated from the University of Florida with a Bachelors Degree in Pharmacy.

I have been involved in research and development relating to pharmacology, and particularly anesthetics, since 1986, and consider myself an expert in this field.

I am familiar with the subject matter and prosecution history of the above-identified application, including the Office Action dated June 05, 2002.

I have been personally involved in the development of the presently claimed compounds and am personally aware of the following historical events.

I note the Examiner's position in the Office Action dated June 5, 2002, that Sipos and Castillo combined teach the method according to the present invention.

The following experimentation was conducted by me, or under my direct supervision.

PROCEDURE

I was prepared to conduct a comparative experimentation to demonstrate that neither the Sipos or Castillo references teach an anesthetic that can be evaporated.

At the beginning, the basic idea was to perform an evaporation test in the Sipos formulation, the Castillo formulation, and the formulation of the present invention, and compare the results of the three tests.

The first step of the present experiment was the preparation of the formula disclosed in the Sipos patent.

Formulas in the Sipos patent require a cyclic alcohol in a base with ethanol and water. The only cyclic alcohol that we were able to obtain was 2-methyl-cyclohexanol (2MC). This chemical is hydrophobic,

and, therefore, requires an emulsion to be made with ethanol and/or water.

The undersigned, and a group of his experienced laboratory staff, attempted to reproduce the Formulation of the Sipos reference disclosed in examples 7 and 10.

As follows, please find some of the formulas that were attempted:

Ingredient	qty units	
ALCOHOL, ISOPROPYL 99%	53.53 ml	Source McKESSON
2-METHYL-CYCLOHEXANOL Date: N/A	6 ml	Lot QD1268 Exp Source SPECTRUM
water, distilled	33 ml	Source Crystal Springs
Lidocaine Usp, Date: 09-05	8 gm	Lot 81110024 Exp Source SPECTRUM
BOTTLE 4OZ GLASS AMBER	1 ea	Lot Source McKESSON

DISSOLVE THE LIDOCAINE IN THE ALCOHOL THE ADD THE 2-METHYL-CYCLOHEXANOL THEN ADD THE WATER

Ingredient	qty	units	
ALCOHOL, GRAIN 95%	52.63	ml	Source
2-METHYL-CYCLOHEXANOL Date: N/A	12	ml	Lot QD1268 Exp Source SPECTRUM
water, distilled	30	ml	Source Crystal Springs
Lidocaine Usp, Date: 09-05	8	gm	Lot 81110024 Exp Source SPECTRUM
BOTTLE 4OZ GLASS AMBER	1	ea	Lot Source McKESSON

DISSOLVE THE LIDOCAINE IN THE ALCOHOL THEN ADD THE 2-METHYL-CYCLOHEXANOL.

In both cases, it was observed that the 2MC separated from the water phase, producing two immiscible phases. **Thus, a homogeneous formulation could not be obtained.**

After consulting with my laboratory staff, we took the decision of adding to the Sipos formulation surfactants in order to mix the two phases and produce a homogenous formulation. The addition of the surfactants only slightly delayed the separation of the phases, but after a couple of minutes, the phases were separate.

Ingredient	qty	units	
ALCOHOL, GRAIN 95%	52.63	ml	Source
2-METHYL-CYCLOHEXANOL Date: N/A	12	ml	Lot QD1268 Exp Source SPECTRUM
water, distilled	30	ml	Source Crystal Springs
SODIUM CHLORIDE USP GRANULAR Date: 06/30/2007	8	gm	Lot 64350 Exp Source PCCA
BOTTLE 4OZ GLASS AMBER	1	ea	Lot Source McKESSON

DISSOLVE THE SODIUM CHLORIDE IN THE WATER.
DISSOLVE THE 2-METHYL-CYCYLHEXANOL IN THE ALCOHOL
COMBINE THE TWO MIXTURES

Ingredient	qty	units	
ALCOHOL, GRAIN 95%	52.63	ml	Source
PROPYLENE GLYCOL, USP Date: NONE	10	ml	Lot 9G6753 Exp Source McKesson
2-METHYL-CYCLOHEXANOL Date: N/A	12	ml	Lot QD1268 Exp Source SPECTRUM
water, distilled	24	ml	

		Source Crystal Springs
Lidocaine Usp, Date: 09-05	4 gm	Lot 81110024 Exp
		Source SPECTRUM
BOTTLE 4OZ GLASS AMBER	1 ea	Source McKESSON

DISSOLVE THE LIDOCAINE IN THE ALCOHOL
THEN ADD THE PROPYLENE GLYCOL AND THE 2-METHYL-CYCLOHEXANOL
ADD THE WATER.

Ingredient	**qty units**	
ALCOHOL, ISOPROPYL 99%	50.5 ml	Source McKESSON
2-METHYL-CYCLOHEXANOL Date: N/A	12 ml	Lot QD1268 Exp
		Source SPECTRUM
water, distilled	30 ml	Source Crystal Springs
SODIUM CHLORIDE USP GRANULAR Date: 06/30/2007	8 gm	Lot 64350 Exp
		Source PCCA
BOTTLE 4OZ GLASS AMBER	1 ea	Lot Source McKESSON

DISSOLVE THE SODIUM CHLORIDE IN THE WATER
ADD THE 2-METHYL-CYCLOHEXANOL TO THE ALCOHOL
MIX THE TWO LIQUIDS

The undersigned and his experienced laboratory staff used all their knowledge trying to mix the two phases without any success.

The next step was trying to obtain the product directed from the company, which owns the patent "Johnson & Johnson."

The undersigned and his legal representative searched for over five hours on the Internet trying to obtain the product protected by the patent. The Johnson & Johnson website, as well as all the companies affiliated with Johnson & Johnson, were searched without any success.

A search, based on the chemicals disclosed by the Sipos patent, was also performed without any success.

At this point, the undersigned believes that Sipos was not able to release a product to the market based on US Patent No. 4,091,090 because he encountered the same problems encountered by the undersigned and his staff.

The undersigned believes that the Sipos formulation was never released to the market because the formulation is **non- operative.**

The second step of the experiment was to conduct an evaporation test with the formulation of the Castillo reference and the formulation of the present invention.

The Castillo formulation as follows:

BETACAINE PLUS OINT. 100 gm

Ingredient	qty units	
Lidocaine Usp, Date: 09-05	15 gm	Lot 81110024 Exp Source SPECTRUM
Prilocaine (base)	5 ml	Source Compounded
WAX, PARAFFIN, WHITE, CAKE	5 gm	Source MEDISCA
petrolatum, white	75 gm	Source SPECTRUM
TUBE COLLAPSIBLE PLASTIC 1 OZ	3.333 ea	Source PCCA

HEAT PETROLATUM TO 45 C. DISSOLVE LIDOCAINE AND WAX IN PETROLATUM. ADD THE PRILOCAINE TO THIS MIXTURE. LET COOL WHILE MIXING.

The formulation of the present invention as follows:

BETACAINE ENHANCED GEL 100 gm

Ingredient	qty units	
CARBOPOL 940 SPECTRUM Date: 04/05	1.046 gm	Lot QA0934 Exp Source SPECTRUM
water, distilled	29.421 ml	Source Crystal Springs
ALCOHOL, ISOPROPYL 99%	66.286 ml	

		Source McKESSON
POLYSORBATE 80 Date: NONE	.986 ml	Lot 82099 Exp
		Source PCCA
Lidocaine Usp, Date: 09-05	5 gm	Lot 81110024 Exp
		Source SPECTRUM
petrolatum, white	12.392 gm	
		Source SPECTRUM
TUBE COLLAPSIBLE PLASTIC 1 OZ	3.333 ea	
		Source CANADA

DISSOLVE CARBOPOL IN HOT WATER(45 C-50 C). MIX WELL TO DISPERSE ALL THE CARBOPOL.

THERE SHOULD BE NO VISIBLE LUMPS OF CARPOBOL. ADD PS 80 IN SMALL AMOUNTS WHILE MIXING VIGOROUSLY.

HEAT PETROLATUM TO 45 C. DISSOLVE LIDOCAINE IN PETROLATUM. ADD THIS MIXTURE TO THE CARBOPOL,

PS 80, AND WATER MIXTURE. MIX WELL. SLOWLY ADD THE ALCOHOL TO THIS MIXTURE WHILE VIGOROUSLY MIXING.

Ten grams of each formulation were placed on glassine paper and then spread out so that each sample had the same surface area. The results are as follows:

	Weight (gm)	
Time (min)	Betacaine Plus Castillo reference	Betacaine Gel Present invention
5	9.999	9.289
10	9.999	8.718
15	9.998	8.037
20	9.998	7.348
30	9.996	7.035
45	9.996	5.52
60	9.996	4.943
90	9.996	4.3
1020	9.996	2.19

As can be seen from the results of the test, the formulation of the Castillo reference DOES NOT evaporate.

The formulation of the present invention rapidly evaporates.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and

belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application of any patent issuing thereon.

Date: 11-27-02

James Castillo